Notice of Allowability	Application No.	Applicant(s)	
	10/035,349	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *draft response of 07 October 2004 and interview of 17 November 2004*.

2. ☒ The allowed claim(s) is/are *1-47,52 and 56-58*.

3. ☒ The drawings filed on *15 April 2002* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit: 1634

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. Authorization for this examiner's amendment was given in a telephone interview with Kenneth E. Jenkins, Ph.D., Registration Number 51,846, on 17 November 2004.

The application has been amended as follows:

1. (Currently Amended) A method for sequencing a terminal portion of an oligomer, comprising:

(a) contacting said oligomer with a mass defect labeling moiety to covalently attach the mass defect labeling moiety to a terminus of the oligomer and form a labeled oligomer, said mass defect labeling moiety comprising at least one element having an atomic number from 17 to 77~~, with the proviso that said element is other than sulfur or phosphorus~~;

(b) fragmenting said labeled oligomer using an enzymatic, chemolytic or mass spectrometric fragmentation method to produce labeled oligomer fragments;

(c) identifying a mass spectrum data corresponding to said labeled oligomer fragments; and

(d) determining the sequence of at least two terminal residues of said labeled oligomer, wherein said sequence determination step comprises discriminating between the mass of the labeled oligomer fragment and an unlabeled oligomer fragment based on the nuclear binding energy of the mass defect labeling moiety ~~is based at least in part on the mass defect of said labeling moiety, wherein said mass defect is less than 1 amu;~~

wherein said oligomer is selected from the group consisting of a protein, polysaccharide, nucleic acid, and lipid.

9. (Currently Amended) The method of claim 1, wherein said oligomer is ~~selected from the group consisting of~~ a protein~~, an oligonucleotide, an oligosaccharide and a lipid~~.

10. (Currently Amended) The method of claim ~~9~~ 1, wherein said oligomer is ~~an oligonucleotide~~ a polysaccharide.

13. (Currently Amended) The method of claim 1, wherein several oligomers, each labeled with a different number of mass defect ~~elements~~ labeling moieties are mixed prior to said fragmenting or analyzing step.

14. (Currently Amended) A method for sequencing a portion of an oligomer in an oligomer mixture, said method comprising:

(a) contacting said oligomer mixture with a ~~terminus~~ mass defect labeling moiety to covalently attach the ~~terminus~~ mass defect labeling moiety to a terminus of said oligomer and form a labeled oligomer mixture, said ~~terminus~~ mass defect labeling moiety comprising at least one element having an atomic number from 17 to 77~~, with the proviso that said element is other than sulfur or phosphorus~~;

(b) separating individual labeled oligomers in said labeled oligomer mixture; ~~and~~

(c) identifying a mass spectrum data corresponding to said individual labeled oligomer; and

(d) analyzing said mass spectrum data to determine the sequence of at least two terminus residues of said oligomer, wherein said analysis step comprises discriminating between the mass of the labeled oligomer and an unlabeled oligomer based on the nuclear binding energy of the mass defect labeling moiety ~~is based at least in part on the mass defect of said labeling moiety, wherein said mass defect is less than 1 amu,~~

wherein said oligomer is selected from the group consisting of a protein, polysaccharide, nucleic acid, and lipid.

23. (Currently Amended) A method for structure and function analysis of an oligomer having a plurality of residues, said method comprising:

(a) contacting said oligomer with a mass defect labeling reagent to differentially label exposed residues and unexposed residues and produce a differentially labeled oligomer comprising a mass defect labeling moiety, wherein said mass defect labeling reagent comprises at least one element having an atomic number of from 17 to 77 that is other than sulfur or phosphorus;

(b) identifying a mass spectrum data corresponding to said differentially labeled oligomer; and

(c) analyzing said mass spectrum data to determine sequences of said oligomer that are exposed in the three-dimensional structure and sequences of said oligomer that are unexposed in the three-dimensional structure, wherein said analysis step comprises discriminating between the mass of the differentially labeled oligomer and an unlabeled oligomer based on the nuclear binding energy of the mass defect labeling moiety ~~is based at least in part on the mass defect of said labeling moiety, wherein said mass defect is less than 1 amu,~~

wherein said oligomer is selected from the group consisting of a protein, polysaccharide, nucleic acid, and lipid.

24. (Presently Amended) A method in accordance with claim 23, wherein said oligomer is a protein~~, a nucleic acid, or an oligosaccharide~~.

26. (Original) A method in accordance with claim ~~26~~ 23, wherein said mass defect labeling reagent is bromine and said oligomer is a protein.

32. (Currently Amended) A method for sequencing the terminal portion of an oligomer, comprising:

(a) contacting a first sample of said oligomer with a labeling moiety to covalently attach a label to the terminus of the oligomer and form a labeled oligomer, said labeling moiety having one element with an atomic number from 17 to 77~~, with the proviso that said element is other than sulfur or phosphorus~~;

(b) contacting a second sample of said oligomer with a labeling moiety to covalently attach a label to a terminus of the oligomer and form a labeled oligomer, said labeling moiety having two elements with an atomic number from 17 to 77, ~~with the proviso that said elements are other than sulfur or phosphorus~~;

(c) optionally, repeating step (b) from one to three times with additional samples, wherein the labeling moieties have three, four or five elements, respectively, with an atomic number from 17 to 77, ~~with the proviso that said elements are other than sulfur or phsophorus~~;

(d) mixing the labeled oligomers from steps (a) through (c);

(e) fragmenting said labeled oligomers using an enzymatic, chemolytic or mass spectrometric fragmentation method to produce labeled oligomer fragments;

(f) identifying a mass spectrum data corresponding to said labeled oligomer fragments; and

(g) determining the sequence of at least two terminal residues of said labeled oligomer fragments, wherein said sequence determination step comprises discriminating between the mass of the labeled oligomer fragment and an unlabeled oligomer fragment based on the nuclear binding energy of the labeling moiety ~~is based at least in part on the mass defect of said labeling moiety, wherein said mass defect is less than 1 amu;~~

wherein said oligomer is selected from the group consisting of a protein, polysaccharide, nucleic acid, and lipid.

36. (Currently Amended) The method of claim 32, wherein each of said elements is selected from the group consisting of bromine, iodine, europium and yttrium and said oligomer is ~~an oligonucleotide~~ a nucleic acid.

37. (Currently Amended) The method of claim 32, wherein each of said elements is selected from the group consisting of bromine, iodine, europium and yttrium and said oligomer is ~~an oligosaccharide~~ a polysaccharide.

38. (Currently Amended) A method for sequencing a portion of an oligomer, comprising:

(a) fragmenting aliquots of said oligomer using one or more specific enzymatic or chemolytic fragmentation methods to produce oligomer fragments, wherein a different fragmentation method is applied to each aliquot;

(b) contacting a first aliquot of oligomer fragments with a first labeling moiety to covalently attach said first labeling moiety to a terminus of the oligomer fragments and form labeled oligomer fragments, said first labeling moiety having one element with an atomic number from 17 to 77~~, with the proviso that said element is other than sulfur or phosphorus~~;

(c) optionally contacting the other aliquots of oligomer fragments with other distinct labeling moieties to covalently attach said distinct labeling moieties to the termini of the oligomer fragments and form labeled oligomer fragments, said distinct labeling moiety having two or more elements with an atomic number from 17 to 77~~, with the proviso that said elements are other than sulfur or phosphorus~~;

(d) optionally mixing the aliquots of labeled oligomer fragments;

(e) identifying a mass spectrum data corresponding to said labeled oligomer fragments; and

(f) determining the sequence of at least two residues of said labeled oligomer, wherein said sequence determining step comprises discriminating between the mass of the labeled oligomer fragments and an unlabeled oligomer fragment based on the nuclear binding energy of the labeling moiety ~~is based at least in part on the mass defect of said labeling moiety, wherein said mass defect is less than 1 amu,~~

wherein said oligomer is selected from the group consisting of a protein, polysaccharide, nucleic acid, and lipid.

42. (Currently Amended) A method in accordance with claim 38, wherein said oligomer is ~~an oligosaccharide~~ a polysaccharide.

45. (Currently Amended) A method for comparing the relative abundances of analytes from two or more samples, comprising:

(a) contacting the analytes of the first sample with a labeling moiety to covalently attach a label to the analytes and form labeled analytes, said labeling moiety having

one element with an atomic number from 17 to 77~~, with the proviso that said element is other than sulfur or phosphorus~~;

(b) contacting the analytes of subsequent samples with labeling moieties to covalently attach labels to the analytes in each sample, wherein the labeling moieties used for each subsequent sample contain an additional element with an atomic number from 17 to 77~~, with the proviso that said elements are other than sulfur or phosphorus~~;

(c) mixing the aliquots of labeled analytes;

(d) identifying mass spectrum data corresponding to said labeled analytes; and

(e) analyzing said mass spectrum data to determine the relative abundances of one or more of the analytes between the samples, wherein said analysis step comprises discriminating between the mass of the labeled analytes and an unlabeled analyte based on the nuclear binding energy of the labeling moiety ~~is based at least in part on the mass defect of said labeling moiety, wherein said mass defect is less than 1 amu~~

wherein said analyte is selected from the group consisting of a protein, polysaccharide, nucleic acid, and lipid.

Cancel claims 48-51.

Cancel claims 53-55.

56. (Currently Amended) The method of claim 52, wherein said stable isotope is [selected from the group consisting of ^{2}H, ^{13}C, ^{15}N and] ^{81}Br.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

4. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

5. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
17 November 2004